Netupitant/palonosetron for prevention of nausea and vomiting: Added benefit not proven

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The German Institute for Quality and Efficiency in Health Care (IQWiG) examined in a dossier assessment whether the drug combination netupitant/palonosetron (trade name: Akynzeo) offers an added benefit over the appropriate comparator therapy (ACT). The drug combination has been approved since May 2015 for the prevention of acute and delayed nausea and vomiting in adult patients receiving moderately or highly emetogenic (vomit-inducing) cancer chemotherapy. According to the findings, such an added benefit is not proven in moderately emetogenic or in highly emetogenic chemotherapeutic regimens.

Appropriate comparator therapy depends on type of chemotherapy

The Federal Joint Committee (G-BA) distinguished between two treatment situations in its commission: In moderately emetogenic chemotherapy, the added benefit of the new drug combination was to be examined in comparison with a dual combination of a serotonin antagonist and dexamethasone as ACT. In cisplatin-based chemotherapy, which is highly emetogenic, the specified ACT consisted of a triple combination, namely a serotonin antagonist, a neurokinin-1 receptor antagonist and, again, dexamethasone.

No evaluable data on moderately emetogenic chemotherapy

For the first research question (moderately emetogenic chemotherapy), the drug manufacturer presented data in its dossier from a study of direct comparison and from an indirect comparison, in which palonosetron had been used as serotonin antagonist. Both comparisons are unsuitable for the derivation of the added benefit because the study of direct comparison, which was also used for the indirect comparison, included patients receiving a combination chemotherapy classified as highly emetogenic in current guidelines.

In highly emetogenic chemotherapy, certain advantages only in side effects

For the second research question (highly emetogenic cisplatin-based chemotherapy), the manufacturer chose the triple combination palonosetron, aprepitant and dexamethasone from the allowed ACTs. In one relevant study (NETU-10-29), this drug combination had been compared with netupitant/palonosetron and dexamethasone in patients receiving moderately emetogenic chemotherapy and in patients receiving highly emetogenic chemotherapy. The analyses submitted in the dossier were conducted on the basis of the second subpopulation, which was relevant for the research question. The assessment was conducted based on the results during the entire study duration, i.e. across several cycles of chemotherapy.

There was no statistically significant difference and therefore no hint of an added benefit of netupitant/palonosetron versus the comparator therapy for the outcomes "all-cause mortality", "serious adverse events" and "treatment discontinuation due to adverse events". Health-related quality of life was not investigated, and there were no evaluable data for

the outcome "nausea". Hence an added benefit is not proven for these 2 outcomes either.

For the outcome "vomiting", the manufacturer only presented results for the first chemotherapy cycle. These were inadequate for the derivation of an added benefit, particularly because mainly anti-emetogenic effects that last for several chemotherapy cycles are relevant for patients.

There was a statistically significant difference in favour of netupitant/palonosetron for the harm outcome "diarrhoea", and hence a hint of considerably lesser harm in comparison with the triple combination.

On its own, this positive effect regarding side effects cannot be interpreted in a meaningful way, however: Proof of equivalence in other outcome categories would be additionally required for the derivation of an added benefit. No data or no evaluable data or no sufficient data were available for this, however. Hence an added benefit of netupitant/palonosetron in comparison with the ACT is not proven for adult patients receiving highly emetogenic chemotherapy in the prevention and treatment of nausea and vomiting.

More information: www.iqwig.de/download/A15-28_N … ertung-35a-SGB-V.pdf

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